

Attorney Docket No: 60019190-1038

AMENDMENTS TO THE SPECIFICATION

Please insert the following paragraph at page 3, line 11, before the third paragraph:

The crystal structure of testicular ACE (tACE) has been described. (Natesh et al., *Crystal structure of the human angiotensin-converting enzyme-lisinopril complex*, Nature 421:551 (2003)). Natesh et al. describe and show an illustration of a ribbon model of tACE with an inhibitor, lisinopril, bound to the active site (Figure 1). The structure includes a lid formed by helices $\alpha 1$ and $\alpha 2$, and indicates the position of seven evolutionarily conserved cysteines. Two cysteines and their associated β -sheets are also indicated. A cysteine at the right of the structure illustration links helix $\alpha 17$ to helix H7. A side wall formed by $\beta 4$ and $\beta 5$ is next to the active site, as indicated by lisinopril.

Please insert the following paragraph at page 3, line 16, after "(Fig. 3 [5])", and before "Thus" :^o

Figure 3 shows and in silico reduction of tACE: conversion of one cysteine to an alanine. "Reduction" of the middle cysteine of tACE removes a side wall of the active site. C352 and C370 in Figure 3 correspond to C383 and C401, respectively, in the numbering scheme of the tACE precursor (SwissProt P22966).

Please insert the following paragraph at page 5, line 18, at the of the third paragraph after "(Fig. 4b)":

Figure 4b shows somatic ACE showing complementarity of the N- and C-channel domains. The secretase, an integral member protein associated with sACE, may have a chaperone-like function to hold the two domains of sACE together.

Please insert the following paragraph at page 5, line 26, after "(Fig. 6)":

Figure 6 shows the disulfide isomerase reaction possible at the heart of the disulfide zipper which might convert sACE into a kind of reciprocating enzyme.

Please insert the following paragraph at page 16, line 8, after the first paragraph:

Figure 10, for example, is a schematic illustration of sACE on one immunocyte (T-cell, monocyte/macrophage, or endothelial cell) binding to sACE on another immunocyte so as to promote specific cell-cell interactions. White triangle, "lid" formed by alpha helices $\alpha 1$ and $\alpha 2$; N and C, termini of each domain.

Attorney Docket No: 60019190-1038

At page 16, line 22, please delete "Fig. 11".

Please insert the following paragraph at page 16, line 29, before the last paragraph:

For example, a prompt response to angiotensin II receptor blockade was observed in a first subject, a 33-year-old white male subject with psoriasis. The subject presented with classic symptoms of psoriasis on the skin of his back and nails of his hands, including scaly reddened patches of epidermis on his back and discolored, raised nails. After three weeks of treatment with valsartan at 80 mg daily, the subject showed clear improvement of symptoms on both the epidermis on his back and nails. A second subject, a 62-year-old white male with chronic psoriasis was taking 75 mg of methotrexate daily for treatment. After taking 200 mg/day of quinapril for two months, the subject was able to stop his methotrexate treatment.

At page 48, in the BRIEF DESCRIPTION OF THE FIGURES section:

Please delete lines 25 - 26 referring to Figures 11 a- g.

At line 27, please delete "12" after "Figure" and insert "11" therefor.